

We claim:

1. A method for preventing and/or treating a disease selected from the group consisting of the systemic inflammatory response syndrome, sepsis, septic shock, thrombus formation in the micro-vasculature and disseminated intravascular coagulation in a mammal by administering a partial inhibitor of factor VIII to the said mammal.
5
2. A method for restoring the plasma level of anti-thrombin and/or activated protein C and/or tissue factor pathway inhibitor in a mammal by administering a partial inhibitor of factor VIII to the said mammal.
10
3. A method according to claim 1, wherein the partial inhibitor of factor VIII is a ligand, being other than a polyclonal antibody, able to only partially inactivate factor VIII or a complex involving factor VIII when the said ligand is in a physiological excess by binding to a site of factor VIII or the said complex.
15
4. A method according to claim 1, wherein the partial inhibitor of factor VIII is a ligand which is able to inactivate the co-factor activity of factor VIII by interfering with a proteolytic cleavage site or the von Willebrand factor or the tenase complex reaction or by inducing a three-dimensional conformational change in factor VIII or by targeting a domain of factor VIII, in particular the C1 domain of factor VIII, or by targeting factor VIII in the factor VIII-von Willebrand factor complex.
20
- 25
5. A method according to claim 1, wherein the partial inhibitor of factor VIII is a human monoclonal antibody obtainable from the cell line named KRIX 1 deposited with the Belgian Coordinated Collections of Micro-organisms under accession number LMBP 5089CB, or from a cell line producing human monoclonal antibodies having a reactivity substantially identical to that of the human monoclonal antibodies obtained from the cell line KRIX 1.
30
6. A method according to claim 1, wherein the partial inhibitor of factor VIII is of class IgG.
35
7. A method according to claim 1, wherein the partial inhibitor of factor VIII is

able to recognize epitopes located in the C1 domain of factor VIII.

8. A method according to claim 1, wherein the partial inhibitor of factor VIII is
5 a monoclonal antibody produced by on purpose immunization in animals,
preferably in mouse.
9. A method according to claim 1, wherein the partial inhibitor of factor VIII is
10 able to bind to a site which is at a predetermined distance of a
physiologically functional site of factor VIII.
10. A method according to claim 1, wherein the partial inhibitor of factor VIII is
15 a humanized monoclonal antibody.
11. A method according to claim 1, wherein the partial inhibitor of factor VIII
20 ligand is an antigen-binding fragment Fab, Fab' or F(ab')₂, a
complementarity determining region, a soluble or membrane-anchored
single-chain variable part, a single variable domain or a derivative of a
human monoclonal antibody obtainable from the cell line named KRIX 1
25 deposited with the Belgian Coordinated Collections of Micro-organisms
under accession number LMBP 5089CB, or from a cell line producing
human monoclonal antibodies having a reactivity substantially identical to
that of the human monoclonal antibodies obtained from the cell line KRIX
1.
12. A method according to claim 1, wherein the partial inhibitor of factor VIII is
30 administered in an anti-thrombin and/or activated protein C and/or tissue
factor pathway inhibitor plasma level restoring amount.
13. A pharmaceutical composition for the prevention and/or treatment of a
35 disease selected from the group consisting of the systemic inflammatory
response syndrome, sepsis, septic shock, thrombus formation in the
microvasculature and disseminated intravascular coagulation in mammals,
comprising as an active ingredient a partial inhibitor of factor VIII, being
able to only partially inactivate factor VIII or a complex involving factor VIII
when the said ligand is in a physiological excess by binding to a site of
factor VIII or the said complex, in admixture with a pharmaceutically
acceptable carrier.

14. A pharmaceutical composition according to claim 13, wherein the partial inhibitor of factor VIII is a ligand other than a polyclonal antibody.

5 15. A pharmaceutical composition according to claim 13, wherein the only partial inactivation by the said active ingredient of factor VIII or of a complex involving factor VIII is an at most 99% inactivation.

10 16. A pharmaceutical composition according to claim 13, wherein the only partial inactivation, by the said active ingredient, of factor VIII or of a complex involving factor VIII is an at least 25% inactivation.

15 17. A pharmaceutical composition according to claim 13, wherein the partial inhibitor of factor VIII is present in an anti-thrombin and/or activated protein C and/or tissue factor pathway inhibitor plasma level restoring amount.

20 18. A pharmaceutical composition according to claim 13, further comprising a therapeutically effective amount of an anti-thrombotic agent.

25 19. A pharmaceutical composition according to claim 13, further comprising a therapeutically effective amount of heparin.

30 20. A method according to claim 1, further comprising the sequential administration of a therapeutically effective amount of an anti-thrombotic agent.

21. A method according to claim 1, further comprising the sequential administration of a therapeutically effective amount of heparin.